Claims

1. A composition comprising a decoy peptide which binds to a neurotoxic β-amyloid peptide and reduces the ability of the neurotoxic β-amyloid peptide to form aggregates which increase calcium influx into neuronal cells.

2. The composition of claim 1 wherein the decoy peptide is non-hydrolyzable.

3. The composition of claim 2 wherein the decoy peptide is selected from the group consisting of peptides comprising D-amino acids, peptides comprising a -psi[CH_2NH]- reduced amide peptide bond, peptides comprising a -psi[$COCH_2$]- ketomethylene peptide bond, peptides comprising a -psi[CH(CN)NH]- (cyanomethylene)amino peptide bond, peptides comprising a -psi[$CH_2CH(OH)$]- hydroxyethylene peptide bond, peptides comprising a -psi[CH_2O]- peptide bond, and peptides comprising a -psi[CH_2S]- thiomethylene peptide bond.

4. The composition of claim 1 wherein the neurotoxic β-amyloid peptide is selected from the group consisting of βAP_{1-42} and βAP_{25-35}.

5. The composition of claim 1 wherein the decoy peptide has β sheet forming potential.

6. The composition of claim 5 wherein the decoy peptide is between 4 and 20 amino acids in length.

7. The composition of claim 6 wherein the decoy peptide is between 5 and 10 amino acids in length.

8. The composition of claim 5 wherein the decoy peptide is a cyclized peptide.

9. The composition of claim 4 wherein the decoy peptide comprises a sequence selected from the group consisting of amino acids 1-6 of SEQ ID NO:1, amino acids 1-6 of SEQ ID

NO:2, amino acids 1-6 of SEQ ID NO:3, amino acids 1-6 of SEQ ID NO:4, amino acids 1-6 of SEQ ID NO:5, amino acids 1-6 of SEQ ID NO:6, amino acids 1-6 of SEQ ID NO:7, amino acids 1-6 of SEQ ID NO:8, amino acids 1-9 of SEQ ID NO:9, amino acids 1-7 of SEQ ID NO:12, amino acids 1-7 of SEQ ID NO:13, amino acids 1-7 of SEQ ID NO:14, amino acids 1-6 of SEQ ID NO:15, amino acids 1-5 of SEQ ID NO:16, amino acids 1-9 of SEQ ID NO:17, amino acids 1-9 of SEQ ID NO:18, amino acids 1-7 of SEQ ID NO:19, amino acids 1-5 of SEQ ID NO:21, amino acids 1-5 of SEQ ID NO:22, amino acids 1-5 of SEQ ID NO:23, amino acids 1-5 of SEQ ID NO:24, amino acids 1-5 of SEQ ID NO:25, amino acids 1-5 of SEQ ID NO:26, amino acids 1-5 of SEQ ID NO:27, amino acids 1-6 of SEQ ID NO:28, amino acids 1-6 of SEQ ID NO:29, and amino acids 1-6 of SEQ ID NO:30.

10. The composition of claim 9 wherein the decoy peptide comprises a sequence selected from the group consisting of amino acids 1-6 of SEQ ID NO:2, amino acids 1-6 of SEQ ID NO:9 and amino acids 1-9 of SEQ ID NO:17.

11. The composition of claim 1 wherein the decoy peptide is conjugated to a compound which facilitates transport across the blood-brain barrier into the brain.

12. The composition of claim 11 wherein the compound is selected from the group consisting of a transferrin receptor binding antibody, cationized albumin, Met-enkephalin, lipoidal forms of dihydropyridine, cationized antibodies, and docosohexanoic acid.

13. The composition of claim 1 wherein the neuronal cells are NT2-N cells differentiated with retinoic acid.

14. A method for treating a subject having a condition characterized by neurotoxic β-amyloid peptide aggregates comprising administering to the subject an amount of a decoy peptide which binds to a neurotoxic β-amyloid peptide and reduces the ability of the neurotoxic β-amyloid peptide to form aggregates which increase calcium influx into neuronal cells effective to reduce neurotoxic β-amyloid peptide aggregate formation in the subject.

15. The method of claim 14 wherein the neurotoxic β-amyloid peptide aggregates include β-amyloid peptides selected from the group consisting of βAP_{1-42}, βAP_{1-40}, and βAP_{25-35}.

16. The method of claim 14, wherein the decoy peptide is conjugated to a compound which facilitates transport across the blood-brain barrier into the brain.

17. The method of claim 14, further comprising administering a compound which increases transport across the blood-brain barrier.

18. A method for reducing β-amyloid peptide induced increased neuronal cell calcium influx in a subject, comprising administering to the subject an amount of a compound effective to reduce neuronal cell calcium influx in the subject.

19. The method of claim 18 wherein the compound is a decoy peptide which binds to a neurotoxic β-amyloid peptide and reduces the ability of the neurotoxic β-amyloid peptide to form aggregates which increase calcium influx into neuronal cells.

20. The method of claim 19 wherein the decoy peptide is conjugated to a compound which facilitates transport across the blood-brain barrier into the brain.

21. The method of claim 18 wherein the compound is a non-NMDA channel antagonist.

22. The method of claim 21, further comprising administering a decoy peptide.

23. The method of claim 22, further comprising administering a compound which increases transport across the blood-brain barrier.

24. A pharmaceutical composition comprising an amount of a decoy peptide which binds to a neurotoxic β-amyloid peptide and reduces the ability of the neurotoxic β-amyloid peptide to form aggregates which increase calcium influx into neuronal cells effective to reduce neurotoxic β-amyloid peptide aggregate formation, and a pharmaceutically acceptable carrier.

25. The pharmaceutical composition of claim 24, wherein the decoy peptide is conjugated to a compound which facilitates transport across the blood-brain barrier into the brain.

26. A pharmaceutical composition comprising an amount of a non-NMDA channel antagonist effective to reduce neuronal cell calcium influx, and a pharmaceutically acceptable carrier.

27. The pharmaceutical composition of claim 26, wherein the non-NMDA channel antagonist is selected from the group consisting of 6-cyano-7-nitroquinoxaline-2,3-dione (CNQX), 6,7-dinitroquinoxaline-2,3(1H, 4H)-dione (DNQX), 2,3-dihydroxy-nitro-7-sulfamoyl-benzo[f]quinoxaline (NBQX), 1-(4-chlorobenzoyl)piperazine-2,3-dicarboxylic acid (CBPD), 6,7-dichloro-2(1H)-oxoquinoline-3-phosphonic acid (24c), Evans blue, 2,3-dihydroxy-7-sulfamoyl-benzo[f]quinoxaline (BQX), derivatives of 4-oxo-1,4-dihydroquinoline-2-carboxylic acid at the 6-position, 2-amino-3-[3-(carboxymethoxy)-5-methylisoxazol-4-yl]propionic acid (AMOA), 2-amino-3-[2-(3-hydroxy-5-methylisoxazol-4-yl)-methyl-5-methyl-3-+++oxoisoxazolin-4-yl]propionic acid (AMNH), 1-(4-amino-phenyl)-4-methyl-7,8-methyl-endioxyl-5H-2,3-benzodiazepine (GYKI 52466), 6-(1H-imidazol-1-yl)-7-nitro- 2,3(1H,4H)-quinoxalinedione hydrochloride (YM90K), 1-(4-aminophenyl)- 3-methylcarbamyl-4-methyl-7,8-methylenedioxy-3,4 -dihydro-5H-2,3-benzodiazepine (GYKI 53655), and (-)(3S,4aR,6R,8aR)-6-[2-(1(2)H-tetrazole-5-yl)ethyl]-1,2,3,4,4a,5,6,7,8,8a-decahydroisoquinoline-3-carboxylic acid monohydrate (LY326325).

28. The pharmaceutical composition of claim 24 or 26, further comprising a compound which increases transport across the blood-brain barrier.

29. A method for identifying lead compounds for a pharmacological agent useful in the treatment of conditions associated with β-amyloid peptide (Aβ) aggregation, comprising

forming a mixture comprising a Aβ peptide containing a β-sheet forming domain, a decoy peptide which binds to a neurotoxic β-amyloid peptide, and a candidate

pharmacological agent,

incubating the mixture under conditions which, in the absence of the candidate pharmacological agent, permit the decoy peptide to selectively bind the neurotoxic β-amyloid peptide containing a β-sheet forming domain, and

detecting the selective binding of the neurotoxic β-amyloid peptide containing a β-sheet forming domain by the decoy peptide, wherein reduction of selective binding indicates that the candidate pharmacological agent is a lead compound for a pharmacological agent which disrupts Aβ aggregation.

30. The method of claim 29 wherein the candidate pharmacological agent is a peptide.

31. The method of claim 29 wherein the candidate pharmacological agent is a small organic molecule.

32. A method for identifying lead compounds for a pharmacological agent useful in the treatment of conditions associated with increased neuronal cell calcium influx induced by the presence of β-amyloid peptide (Aβ) aggregates, comprising

providing a neuronal cell loaded with a calcium-sensitive compound which is detectable in the presence of calcium,

forming a mixture comprising a Aβ containing a β-sheet forming domain, and a candidate pharmacological agent,

incubating the mixture under conditions which, in the absence of the candidate pharmacological agent, permit the Aβ to aggregate,

contacting the neuronal cell with the mixture, under conditions which, in the presence of Aβ aggregates, permit influx of calcium into the neuronal cell, and

detecting the calcium-sensitive compound as a measure of the relative presence of calcium in the neuronal cell, wherein detection of a lesser amount of calcium in the neuronal cell than is present when the neuronal cell is contacted with Aβ aggregates indicates that the candidate pharmacological agent is a lead compound for a pharmacological agent which disrupts Aβ aggregation.

33. The method of claim 32 wherein the candidate pharmacological agent is a peptide.

34. The method of claim 32 wherein the candidate pharmacological agent is a non-NMDA channel antagonist.

35. The method of claim 32 wherein the candidate pharmacological agent is a small organic molecule.

36. A method for identifying lead compounds for a pharmacological agent useful in the treatment of conditions associated with increased neuronal cell calcium influx induced by the presence of β-amyloid peptide (Aβ) aggregates, comprising

providing a neuronal cell loaded with a calcium-sensitive compound which is detectable in the presence of calcium,

contacting the neuronal cell with Aβ aggregates under conditions which permit calcium influx into the neuronal cell,

detecting the calcium-sensitive compound as a measure of calcium influx induced by Aβ aggregates,

contacting the neuronal cell with a candidate pharmacological agent, and

detecting the calcium-sensitive compound as a measure of the relative presence of calcium in the neuronal cell induced by the candidate pharmacological agent, wherein detection of a lesser amount of calcium in the neuronal cell than is present when the neuronal cell is contacted with Aβ aggregates indicates that the candidate pharmacological agent is a lead compound for a pharmacological agent which reduces Aβ aggregate induced neuronal cell calcium influx.

37. The method of claim 36 wherein the candidate pharmacological agent is a peptide.

38. The method of claim 36 wherein the candidate pharmacological agent is a non-NMDA channel antagonist.

39. The method of claim 36 wherein the candidate pharmacological agent is a small

organic molecule.

40. A method for identifying lead compounds for a pharmacological agent useful in the treatment of conditions associated with increased neuronal depolarization induced by the presence of β-amyloid peptide (Aβ) aggregates, comprising

providing a neuronal cell in a medium containing a potentiometric compound, wherein the influx into the neuronal cell of the potentiometric compound upon depolarization of the neuronal cell is detectable,

forming a mixture comprising a Aβ containing a β-sheet forming domain, and a candidate pharmacological agent,

incubating the mixture under conditions which, in the absence of the candidate pharmacological agent, permit the Aβ to aggregate,

contacting the neuronal cell with the mixture, under conditions which, in the presence of Aβ aggregates, permit influx of a control amount of the potentiometric compound into the neuronal cell, and

detecting the potentiometric compound as a measure of the relative depolarization of the neuronal cell, wherein detection of a lesser amount of potentiometric compound in the neuronal cell than is present when the neuronal cell is contacted with Aβ aggregates indicates that the candidate pharmacological agent is a lead compound for a pharmacological agent which disrupts Aβ aggregation.

41. The method of claim 40 wherein the candidate pharmacological agent is a peptide.

42. The method of claim 40 wherein the candidate pharmacological agent is a small organic molecule.

43. The method of claim 40, wherein the potentiometric compound is fluorescent.

44. The method of claim 43, wherein the potentiometric compound is bis-(1,3-dibutylbarbituric acid)trimethine oxonol ($DiBAC_4(3)$).

45. A method for identifying lead compounds for a pharmacological agent useful in the treatment of conditions associated with increased neuronal depolarization induced by the presence of β-amyloid peptide (Aβ) aggregates, comprising

providing a neuronal cell in a medium containing a potentiometric compound, wherein the influx into the neuronal cell of the potentiometric compound upon depolarization of the neuronal cell is detectable,

contacting the neuronal cell with Aβ aggregates under conditions which permit influx of a control amount of the potentiometric compound into the neuronal cell,

detecting the potentiometric compound in the neuronal cell as a measure of depolarization induced by Aβ aggregates,

contacting the neuronal cell with a candidate pharmacological agent, and

detecting the potentiometric compound in the neuronal cell as a measure of the relative depolarization of the neuronal cell in the presence of the candidate pharmacological agent, wherein detection of a lesser amount of potentiometric compound in the neuronal cell than is present when the neuronal cell is contacted with Aβ aggregates but not the candidate pharmacological agent indicates that the candidate pharmacological agent is a lead compound for a pharmacological agent which reduces Aβ aggregate induced neuronal cell depolarization.

46. The method of claim 45 wherein the candidate pharmacological agent is a peptide.

47. The method of claim 45 wherein the candidate pharmacological agent is a small organic molecule.

48. The method of claim 45, wherein the potentiometric compound is fluorescent.

49. The method of claim 48, wherein the potentiometric compound is bis-(1,3-dibutylbarbituric acid)trimethine oxonol ($DiBAC_4(3)$).